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37 C.F.R. 1.8

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May 20, 2005  
Date

Steven L. Highlander

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

*In re* Application of:

Thomas J. KODADEK

Serial No.: 09/780,575

Filed: February 9, 2001

For: SELECTION OF PEPTIDES WITH  
ANTIBODY-LIKE PROPERTIES

Group Art Unit: 1639

Examiner: Bennett M. Celsa

Atty. Dkt. No.: UTSD:566US/SLH

**DECLARATION OF BRENT IVERSON UNDER 37 C.F.R. §1.116**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

I, Brent L. Iverson, do declare that:

1. I am citizen of the United States residing at 1316 Thaddeus Cove, Austin TX.
  
2. I currently hold the position of Professor in the Department of Chemistry and Biochemistry at the University of Texas-Austin, wherein I have been employed since 1990. In particular, I have been working the field of protein structure and function for 18 years. A copy

of my *curriculum vitae* is attached. In light of my experience, I consider myself to be an expert in the field to which the present invention belongs.

3. I have been asked to review an Office Action advanced against the claims of a patent application, U.S. Serial No. 09/780,575 ("the '575 application"), naming a colleague, Tom Kodadek, as an inventor. In rendering this opinion, I have reviewed the Office Action generally, in particular, Jappelli *et al.*, U.S. Patent 6,365,347 and Dostmann *et al.*, as well as the claims of the '575 application.

4. It is my opinion that, at the time the '575 application was filed, it was not at all clear that one could successfully perform an *in vivo* peptide-peptide library screen to identify very high affinity binding activities. The art cited by the examiner does not address this interaction, but instead, involves the use of *polypeptides* to bind to peptides. One cannot extrapolate from polypeptide-peptide interactions to peptide-peptide interactions. Thus, the examiner's arguments regarding "obviousness" are, I believe, not based on sound scientific reasoning. My opinion is based on the following.

5. First, peptides are distinctly smaller than polypeptides, and hence are less stable from a conformational standpoint. In fact, peptides as a class of molecules do not display any persistent conformations in solution. As a result, both binding partners in the present invention will be subject to conformational instability, thereby rendering it unpredictable whether native interactions (*i.e.*, those where one or both of the peptides is replaced by the related polypeptide) would be preserved due to significant entropic contributions that undermine the overall free

energy of the interaction. A short peptide will only be expected to bind with a high affinity to a cleft within a conformationally well-defined polypeptide such as an antibody or cellular receptor protein.

6. Second, another factor related to the smaller size of peptides, as compared to polypeptides, is that there are fewer opportunities to make molecular contact with the cognate binding partner. Again, as a result, both binding partners in the present invention will be constrained to finding fewer contact points than what is seen in the cited art. This creates another layer of unpredictability that makes it unclear whether native interactions would be preserved.

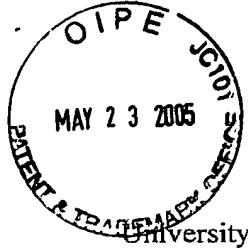
7. I hereby declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the referenced patent application or any patent issued thereon.

5/16/05

Date

NFS.R

Brent L. Iverson, Ph.D.



Brent L. Iverson, Ph.D.  
Warren J. and Viola Mae Raymer Professor  
University Distinguished Teaching Professor, Chemistry and Biochemistry

**A. Professional Preparation**

Institution	Field of Study	Degree	Year
Stanford University, Stanford, California	Chemistry	B.S.	1982
California Institute of Technology, Pasadena, CA	Organic Chemistry	Ph.D.	1987
Research Institute of Scripps Clinic, La Jolla, CA	Biological Chemistry	PostDoc	1989

**B. Appointments**

- 2004-present Warren J. and Viola Mae Raymer Professor, College of Natural Sciences, Department of Chemistry and Biochemistry, the University of Texas at Austin  
2001-present Professor, Department of Chemistry and Biochemistry, the University of Texas at Austin  
1998-present Member of the Institute for Cellular and Molecular Biology, the University of Texas at Austin  
1996-2001 Associate Professor, Department of Chemistry and Biochemistry, Member of the Institute for Cellular and Molecular Biology, The University of Texas at Austin  
1990-1996 Assistant Professor, Department of Chemistry and Biochemistry, The University of Texas at Austin  
1989-1990 Senior Research Associate at Scripps Clinic and Research Foundation  
1987-1989 Postdoctoral Research Fellow at the Scripps Clinic and Research Foundation in the laboratory of Dr. Richard Lerner  
1982-1987 Graduate Research Assistant in the laboratory of Professor Peter Dervan at the California Institute of Technology

**C. Awards**

**Academic and Research Awards:**

- Elected to Phi Beta Kappa, 1982  
American Cancer Society, California Division Postdoctoral Junior Fellowship, 1987-1989  
Camille and Henry Dreyfus Foundation New Faculty Award in Chemistry, 1990  
The Chicago Community Trust Searle Scholars Award, 1991  
National Science Foundation Presidential Young Investigator Award, 1991  
Camille and Henry Dreyfus Foundation Teacher-Scholar Award, 1995  
Alfred P. Sloan Foundation Research Fellow, 1996  
Robert W. Hamilton Best Research Paper Award, 2003  
American Chemical Society Arthur C. Cope Scholar Award, 2005

**Teaching and Service Awards:**

- University of Texas Natural Sciences Advisory Council Teaching Excellence Award, 1993  
The Friar's Centennial Teaching Award, 1994  
Mexican American Health Professions Professor of the Year, 1994  
The Eyes of Texas University Service Award, 1994  
University of Texas Natural Sciences Advisory Council Teaching Excellence Award, 1997  
CIT (Center for Instructional Technology) Faculty Fellow, 1998

Elected to the Academy of Distinguished Teachers, UT Austin, 1999

Texas Ex's Teaching Excellence Award, 2000

Jean Holloway Teaching Excellence Award, 2001

#### D. Selected Recent Publications

- "Recombinant Antibody Fragment Mediated Protection to Anthrax Toxin Challenge Correlates with Antigen Affinity", Maynard, J.A., Leppla, S.H., Brasky, K., Patterson, J.L., Iverson, B.L. and Georgiou, G. *Nature/Biotechnology*, 2002, 20, 597-601.
- "Conformational Modularity of an Abiotic Secondary Structure Motif in Aqueous Solution", Zych, A. and Iverson, B.L. *Helvetica Chimica Acta*, 2002, 85, 3294-3300.
- "Combinatorial Strategies in Biology and Chemistry", Iverson, B.L. *J. Am. Chem. Soc.*; (Book Review), 2002; 124, 12057-12058.
- "Aromatic Oligomers that Form Hetero-duplexes in Water", Gabriel, G. and Iverson, B.L., *J. Am. Chem. Soc.*, 2002; 124, 15174-15175.
- "Viral Assembly of Oriented Quantum Dot Nanowires", Mao, C.; Flynn, C.E.; Hayhurst, A.; Sweeney, R.; Jifa Q, Williams, J.; Georgiou, G.; Iverson, B.L. and Belcher, A.M., *Proc. Nat. Acad. Sci., USA*, 2003, 100, 6946-6951.
- "Isolation and Expression of Recombinant Antibody Fragments to the Biological Warfare Pathogen *Brucella melitensis*" Hayhurst, A., Happea, S., Mabry, R., Kocha, Z., Iverson B.L., Georgiou, G. *Journal of Immunological Methods* 2003, 276 185–196.
- "2,4,6-Trinitrotoluene detection using recombinant antibodies." Goldman, E.R., Hayhurst, A., Lingerfelt, B.M., Iverson, B.L., Georgiou, G., Anderson, G.P. *Journal of Environmental Monitoring*, 2003, 5, 380-383.
- "Synthesis and Organization of Nanoscale II-VI Semiconductor Materials Using Evolved Peptide Specificity and Viral Capsid Assembly", Flynn, Christine E.; Mao, Chuanbin; Hayhurst, Andrew; Williams, Julie L.; Georgiou, George; Iverson, Brent; and Belcher, Angela M. *Journal of Materials Chemistry*, 2003, 13, 2414-2421.
- "Virus-Based Toolkit for the Directed Synthesis of Magnetic and Semiconducting Nanowires", Mao, C., Solis, D., Reiss, B.D., Kottman, S.T., Sweeney, R.Y., Hayhurst, A., Georgiou, G., Iverson, B.L., and Belcher, A.M., *Science*, 2004, 303, 213-217.
- "NMR Structural Analysis of a Modular Threading Tetraintercalator" Lee, J., Guelev, V., Sorey, S., Hoffman, D., and Iverson, B.L., *J. of Am. Chem. Soc.*, 2004, 126, 14036-14042.
- "Anchored Periplasmic Expression, a Versatile Technology for the Isolation of High Affinity Antibodies from *E. coli* Expressed Libraries", Harvey, B.R., Georgiou, G., Hayhurst, A., Jeong, K-J., Iverson, B.L. and Rogers, G.K., *Proc. Nat. Acad. Of Sci, USA*, 2004, 101, 9193-9196.
- "A Periplasmic Fluorescent Reporter Protein and its Application in High-throughput Membrane Protein Toplogy Analysis", Jeong, K.J., Kawarasaki, Y., Gam, J., Harvey, B., Iverson, B., Georgiou, G. *Journal of Molecular Biology*, 2004, 341, 901-909.
- "Bacterial Biosynthesis of Cadmium Sulfide Nanocrystals", Sweeney, R., Mao, C., Gao, X., Burt, J., Belcher, A.M., Georgiou, G., and Iverson, B.L., *Chemistry and Biology*, 2004, 11, 1553-1559.

#### E. Synergistic Activities

Dr. Iverson is an innovator in the classroom as well as the laboratory. He developed a method of teaching organic chemistry that combines standard lecture with computer

animations to emphasize conceptual learning, not simply memorization. He presents seven golden rules of chemistry that are amplified and reinforced throughout the two semester course. He has been recognized with numerous campus-wide teaching awards, and he is a member of the University of Texas Academy of Distinguished Teachers. In recognition of his novel teaching approach, he was recruited to be co-author of the popular Thomson/Brooks-Cole Organic Chemistry textbook along with William Brown and Christopher Foote, now in its 4<sup>th</sup> edition. Dr. Iverson is currently an active member of the Core Curriculum Reform Task Force that was appointed this year by the President of the University to redesign the University's core curriculum required of all undergraduates.